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(54) Treatment of footrot

(57) A veterinary composition for the treatment of ovine footrot, including an effective amount of:
(a) a zinc salt, such as zinc sulphate, and
(b) a fatty thioacid or derivative thereof, such as a lauryl sulphate salt, optionally including an enhancing agent e.g. sodium azide and, if solid, a solubilizing agent. The composition may be topically administered by subjecting animals to a foot bath including the composition in solution, such as in an aqueous solution.

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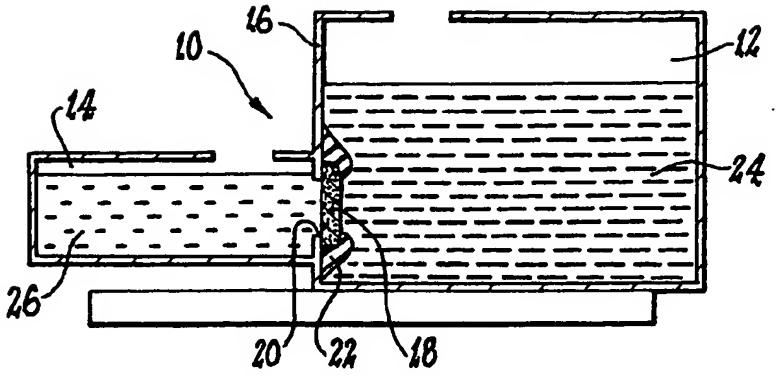

Fig 1

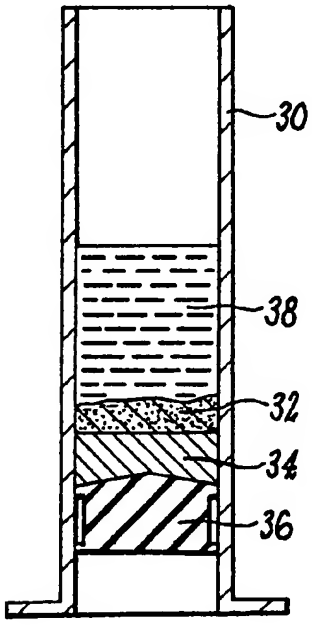

Fig 2

SPECIFICATION

Treatment of Footrot

The present invention relates to a veterinary composition suitable for the treatment of footrot in ovine animals, and to a method of treating footrot utilizing the composition.

Footrot of sheep is a disease of major economic importance in many parts of Australia and New Zealand and in most other sheep raising countries. Indeed the disease was first recognised some 300 years ago. Since the discovery that the disease is caused by a specific organism, Bacteroides nodosus, there have been numerous attempts to produce a therapeutic agent for treatment of the disease. However heretofore to treat footrot by direct application of therapeutic agents, it has been necessary to undertake a thorough footparing before any topical treatment is attempted. That is, it is necessary to expose all infected areas by removing overlying tissues, a very laborious procedure. Moreover, this procedure has proved to be less than completely effective particularly when large flocks of sheep or other animals are bieng treated. This may be due in part to the fact that Bacteroides nodosus can survive for long periods and grow slowly in isolated pockets under the horn.

Accordingly it is an object of the present invention to overcome, or at least alleviate, some of the difficulties related to the prior art.

The present invention accordingly provides a veterinary composition and process for the treatment of footrot. The process is characterised in that it is a topical treatment which does not require footparing.

The present invention provides a veterinary composition including an effective amount of

(a) a zinc salt, and

(b) a fatty thioacid or derivative thereof.

The veterinary composition may further include:

(c) an enhancing agent.

It has been surprisingly discovered that the combination of a zinc salt and a fatty thioacid or derivative thereof provides a veterinary composition which may be topically administered to the hoofs of ovine animals without the necessity for footparing.

The veterinary composition may be in the form of a solution. Alternatively, the veterinary composition may be in the form of a solid. This may later be dissolved in a suitable solvent for use. Preferred solvents include water and alcohols and mixtures thereof. Particularly preferred alcohols include ethanol. A water/ethanol mixture in amounts up to approximately 20% v/v ethanol may be used.

Accordingly zinc salts which are soluble in solution particularly aqueous or alcoholic solution, are preferred. The zinc salts may be selected from zinc acid salts and derivatives thereof. The zinc salts may be selected from zinc halides and derivatives thereof. Preferred zinc acid salts include zinc thioacid salts. The zinc thioacid salts may be selected from one or more of zinc sulphite, zinc sulphate, zinc sulphonate, zinc hydrosulphite, zinc hydrosulphate and derivatives thereof. The zinc acid salts may be used in hydrated form.

The zinc halides may be selected from zinc chloride, zinc bromide, zinc iodide and the oxy halides e.g. zinc perchlorate.

Other zinc salts which may be used include one or more of zinc acetate, zinc nitrate, zinc ammonium chloride, zinc carbonate, zinc borate, zinc ethyl sulphate, zinc phenol sulphonate, zinc salicylate and zinc hydroxyhydrosulphate.

The zinc salts may be present in any suitable effective concentration. The zinc salt may be present in concentrations from about 2% weight/vol. to about 100% weight/vol. Below these concentrations the veterinary composition may not be wholly effective. Above these concentrations difficulties may be encountered with the physical nature of the composition. For solid compositions, the zinc salt may be present in concentrations from about 80% weight/weight of active ingredients to about 98% weight/weight of active ingredients. A concentration of about 90% weight/weight of active ingredients may be used.

The fatty thioacid or derivative thereof may be selected from any suitable compound which will function to potentiate the absorption of zinc ions into the ovine hoof horn. Particularly preferred fatty thioacids are lauric acid derivatives. Lauric sulphate or lauric ether sulphate derivatives have been found to be particularly suitable. Lauryl sulphate salts may be used.

The lauryl sulphate salts may be selected from alkali metal, alkaline earth metal, ammonium and amine salts. The alkali metal or alkaline earth metal lauryl sulphates may be selected from sodium lauryl sulphate, potassium lauryl sulphate or magnesium lauryl sulphate.

The ammonium or amine lauryl sulphates may be selected from ammonium lauryl sulphate, monodi- or tri-ethanolamine lauryl sulphate, triethanolamine ammonium lauryl sulphate, monoisopropylamine lauryl sulphate or mixtures of any of the above.

A corresponding alkali metal, alkaline earth metal, ammonium or amine lauryl ether sulphate may be used instead of or with any of the above specified lauryl sulphate salts.

The fatty thioacids or derivatives thereof may be present in any suitable effective concentration. The concentrations may range from about 0.4% weight/vol. to about 10% weight/vol. A concentration

of approximately 2% weight/vol. may be used. For solid compositions, the fatty thioacids may be present in concentrations of about 2% weight/weight of active ingredients to about 20% weight/weight of active ingredients. A concentration of about 10% weight/weight of active ingredients may be used.

The veterinary compositions according to the present invention may be in the form of solutions, preferably aqueous or alcoholic solutions. In such embodiments, the zinc salts may be used in hydrated form. Zinc sulphate particularly zinc sulphate monohydrate or zinc sulphate heptahydrate may be used.

The veterinary compositions, as stated above, may be present in solid form. The solid form may be later dissolved when required to treat footrot. However it has been found that dissolution in solvents, particularly aqueous solvents may be difficult in certain embodiments.

The solid composition may be dissolved in hot water. However, this may be inconvenient. Moreover, undesirable frothing may occur.

Accordingly the veterinary composition according to the present invention may further include an effective amount of a solubilizing agent. Any suitable veterinarily acceptable solubilizing agent may be utilised. Sulphate salts, particularly bisulphate salts may be used. A preferred solubilizing agent is sodium hydrogen sulphate. The solubilizing agent may be present in amount of from approximately 1% weight/weight of active ingredients to 2% weight/weight of active ingredients.

Where zinc sulphate monohydrate is used as the zinc salt, about 1.9% weight/weight of active ingredients of sodium hydrogen sulphate, based on the weight of zinc salts may be added. For zinc sulphate heptahydrate about 1.2% weight/weight of active ingredients may be added.

The veterinary composition according to the present invention may further include an enhancing agent. An azide compound may be present in the composition according to the present invention. An alkali metal azide compound may be used. Sodium azide is preferred.

Alternatively the enhancing agent may be selected from alcohols, preferably ethanol, or nickel ammonium hydroxide. These compounds have been found to enhance the penetration of zinc ions into hard hoof horn.

It will be understood that in the treatment of footrot, the veterinary composition may be used as a foot bath composition. A suitable composition will consist of zinc sulphate heptohydrate $ZnSO4.7H_2O$; 200 g/L and Sodium lauryl sulphate (dodecyl sodium sulphate) 20 g/l $CH_3(CH_2)_{10}CH_2OSO_3Na(C_{12}H_{25}NaO_4S)$ as an aqueous solution.

The mixture may be prepared at approximately twice the above concentrations with the recommendation that it is diluted with an equal volume of solvent, for example water prior to use.

In accordance with a further aspect of the present invention there is provided a process for the treatment of footrot in ovine animals which includes topically administering a veterinary composition, as described above, to animals requiring such treatment.

The process of the present invention may include subjecting the animals to be treated to a foot bath containing a veterinary composition as described above. The process may be continued for a time sufficient to substantially kill all B nodosus viable organisms. Experiments have shown that at a mean concentration of about 500 ppm (μgm zinc 2+/gm wet weight hoof horn) B nodosus did not grow and could not be recovered as a viable organism from culture plates. Accordingly it is desirable to continue the process of the present invention until concentrations of zinc ion equal to or greater than 400 ppm can be achieved. For example, if feet are treated with a zinc sulphite/sodium lauryl sulphate solution for one hour experiments have shown that concentrations of zinc salt greater than 400 ppm may be achieved.

The process of the present invention may further include repeating the treatment after a pre-determined period. A period of approximately five days has been found to be suitable.

The present invention will now be more fully described with reference to the accompanying examples. It should be understood, however, that the following description is illustrative only and should not be taken in any way as a restriction on the scope of the invention as described above.

EXAMPLE 1

Vitro Testing

Apparatus for in vitro testing is shown in the accompanying drawings, in which:

Figure 1 shows apparatus used for testing penetration of compounds through hoof tissue, and

Figure 2 shows apparatus used for testing uptake of compounds by hoof tissue.

The apparatus of Figure 1 comprises disposable plastic laboratory ware 10, defining a test solution chamber 12 and sampling chamber 14. A common wall 16 separates chambers 12, 14. A hoof sample 18 to be tested is secured in chamber 12, over opening 20 in wall 16, by means of sealer 22.

Hoof samples 18 for testing were obtained from recently slaughtered sheep. Segments of softer tissue from the sole and bulbar sole (heel) and harder tissue from the abaxial proximal area of the hoof was used in all experiments. Each segment was the full thickness of the horn, which varied from 1.3 to 2.4 mm. The segements were fixed in the absorption and penetration apparatus so that the external surface of the segments was in contact with the test solution. A silicone based adhesive (Dow Corning) was used for sealer 22 to attach and seal the hoof segments within the penetration apparatus. The sealer itself was tested to ensure that test agents could not penetrate it. After the sealer had been given

time to set the chamber 12 was filled with the solution 24 under investigation; while saline solution 26 was added to chamber 14. The apparatus was tested for leakage by adding a neutral dye to the test chamber 12 and applying positive pressure and by measuring electrical resistance between the two chambers. For each solution tested in a penetration or absorption experiment a total of eight hoof segments were used, four soft and four hard.

During penetration experiments samples were collected from the sampling chamber 14 at 15 minute intervals for the first hour and at 30 minute intervals thereafter, and were analysed for the compound being investigated. Penetration rate was calculated as the time taken until the compound was first detected in the sampling chamber.

For the absorption tests, the apparatus of Figure 2 was used. That apparatus consisted of a cylindrical, open ended column 30, into which firmly fitted horn segment 32 was pressed so as to bed against soft paraffin 34. The deep surface of segment 32 was pressed into paraffin 34 so as to prevent absorption into that surface. A rubber plunger 36 was provided in the base of column 30 to retain the paraffin.

Hoof horn segments for the absorption studies were cut out of feet with a 1.32 cm leather punch. This fitted firmly into column 30. With the deep surface of a segment 32 pressed into paraffin 34 (Vaseline), 2.5 ml of test solution 38 was then applied to the superficial surface.

In all absorption studies the hoof segments were exposed for one hour to the compound being investigated, then rinsed, digested and analysed for that compound. The samples were digested either by treatment with 10 percent w/v sodium sulphide for 48 hours at room temperature or by heating with a mixture of concentrated nitric, sulphuric and perchloric acids (1:1:1).

The following compounds were tested for penetration and detected by direct spectrophotometric analysis: aminoacridine hydrochloride, chloramphenicol, homidium bromide, squalene, tris-hydroxymethylnitromethan, α-terpineol and tetrahydrofurfuryl alcohol. Chemical colorimetric methods were used to detect sodium axide, sodium borate, sodium bisulphite and metabisulphite, chromium potassium sulphate, copper sulphate, formaldehyde, nickel citrate, salicylic acid, zinc sulphate and benzoic acid. Analysis for copper, chromium and zinc was also carried out using atomic absorption spectrophotometry.

Results

The penetration rates of single compounds in a single solvent are summarized in Table 1. Considerable variability was observed between individual segments of horn. Zinc and copper were the fastest penetrating metal cations and azide was the fastest penetrating anion. Lipophilic compounds penetrated poorly. Formaldehyde failed to penetrate hoof segments even after five days exposure; its penetration rate was therefore less than 0.02 mm per hour.

The effects of other compounds on the penetration rate of azide are summarised in Table 2. Marked increases were also observed with sodium lauryl sulphate and nickel ammonium hydroxide treatments. The keratolytic agents sodium sulphide and sodium thioglycolate increased the penetration rate of azidd, but also had a corrosive effect on the hoof. Niether dimethyl sulphoxide (DMSO) nor urea improved penetration. Penetration was generally better through soft hoof horn than hard hoof horn, except when ethanol or nickel ammonium hydroxide were included in the treatment.

Table 3 summarises the effects of other agents on zinc penetration. Treatment with sodium lauryl sulphate considerably enhanced the penetration of zinc and penetration was further improved if ethanol was also included. With the exception of bisulphite/urea, keratolytic treatments did not greatly increase zinc penetration. As with azide, zinc penetration through hard horn more rapidly than through soft in treatments containing ethanol or nickel ammonium hydroxide.

TABLE 1

Penetration Rates of Single Compounds Through Ovine Hoof Keratin

Compound	Concentration	Solvent	Average Penetration Rate MM/hour	
			Soft Keratin	Hard Keratin
Sodium Azide	5% W/V	H_2O	0.16	0.10
Cupric Sulphate	20% W/V	H_2O	0.17	0.13
Zinc Acetate	15% W/V	H_2O	0.18	—
Zinc Sulphate	20% W/V	H_2O	0.31	0.27

TABLE 2
Effect of Other Compounds on Penetration of Sodium Azide

Compound/s	Concentration	Average Penetration Rate MM/Hour: Soft Keratin	Average Penetration Rate MM/Hour: Hard Keratin
Urea	8M	Insignificant	Insignificant
Sodium Bisulphite	10% W/V	Insignificant	Insignificant
Sodium Bisulphite and Urea	4% W/V 8M	0.39	Insignificant
Sodium Sulphide	5% W/V	0.54	0.43
Thioglycolate pH 10.5	2M	0.44	0.42
Sodium Sulphite	30% W/V	0.15	Insignificant
Ethanol	20% V/V	0.20	0.36
Cuprammonium Hydroxide pH 9.5	5% W/V	0.32	Insignificant
Nickel Ammonium Hydroxide pH 9.5	1.0% W/V	0.34	Insignificant
Nickel Ammonium Hydroxide pH 6.4	1.0% W/V	0.61	0.74
Sodium Lauryl Sulphate	5% W/V	1.02	0.74
Sodium Dodecyl Benzene Sulphosuccinate	5% W/V	Insignificant	Insignificant
Dimethyl Sulphoxide (DMSO)	50% V/V	Insignificant	Insignificant

TABLE 3
Effect of Other Compounds on Penetration of Zinc (as $ZbSO_4 . 7H_2O$ 10% W/V)

Compound	Concentration	Average Penetration Rate MM/Hour: Soft Keratin	Average Penetration Rate MM/Hour: Hard Keratin
Sodium Lauryl Sulphate	2% W/V	1.90	1.05
Sodium Lauryl Sulphate and Ethanol	2% W/V 20% V/V	2.31	3.91
Sodium Dodecyl Benzene Sulphosuccinate	5% W/V	0.66	0.42
Sodium Azide	5% W/V	0.56	0.48
Sodium Lauryl Sulphate and Sodium Azide	2% W/V 1% W/V	1.37	1.31
Sodium Bisulphite and Urea	0.3 M 8 M	0.98	0.81
Thioglycolic Acid pH 3.5	2 M	0.33	Insignificant
Sulphite/Tetrathionate pH 2.5	0.2 M	0.34	Insignificant
Nickel Ammonium Hydroxide pH 6.4	1% W/V	0.46	0.54

TABLE 4
Uptake of Zinc into Ovine Hoof Tissue

Treatment	Zinc Ions (mg/g Hoof Horn) Soft	Hard
Zinc sulphate 10% w/v	0.55	0.36
	0.3—0.67	0.16—0.62
Zinc sulphate 20% w/v	0.59	0.48
	0.44—0.74	0.45—0.51
Zinc hydroxide paste	0.41	0.22
	0.30—0.57	0.16—0.27
Zinc sulphate 10% w/v in 50% DMSO	0.54	0.29
	0.43—0.69	0.12—0.33
Zinc sulphate 10% w/v in formalin 10% v/v	0.06	0.04
	0.01—0.10	0.01—0.07
Zinc sulphate 10% w/v in 2M thioglycollic acid	0.64	0.26
	0.51—0.70	0.15—0.38
Sodium azide 1% w/v	0.53	0.31
	0.49—0.57	0.22—0.41
Sodium lauryl sulphate 4% w/v	0.66	0.40
	0.54—0.70	0.20—0.53
Sodium azide 1% w/v and Sodium lauryl sulphate 2% w/v	0.72	0.40
	0.62—0.85	0.24—0.67
Sodium azide 1% w/v and Sodium lauryl sulphate 2% w/v and ethanol 20% v/v	0.88	0.52
	0.68—0.99	0.41—0.59
Sodium dodecyl sulphosuccinate 2% w/v	0.62	0.30
	0.61—0.62	0.26—0.35
Cetyl trimethylammonium bromide (cetavlon) 1% w/v	0.43	0.34
	0.35—0.55	0.27—0.39
Nickel ammonium hydroxide pH 6.40 5% w/v	0.61	0.68
	0.42—0.96	0.21—1.56

Studies on absorption of zinc by ovine hoof horn are summarised in Table 4. Mean tissue concentrations of 500 μg zinc ions per g and 360 μg zinc ions per g in soft and hard horn respectively were observed after exposing samples to 10 percent w/v $ZnSO_4 . 7H_2O$ solution for one hour. With the exception of formaldehyde the presence of other compounds did not greatly affect the uptake of zinc. The presence of 10 percent v/v formalin decreased absorption to negligible levels. After 24 hours continuous washing of treated hoof segments in running water 85 to 95% of absorbed zinc was retained in soft horn and 50 to 55% was retained in hard horn.

Sodium lauryl sulphate enhanced the penetration of zinc suggesting that this C_{12} alkyl surfactant can increase the rate of penetration of hydrophilic ions such as Zn^{2+} and N_3^- into ovine hoof horn. This effect was not due to the surface active properties of sodium lauryl sulphate alone as neutral, cationic and other anionic detergents did not enhance the penetration of these ions to nearly the same extent. The effect may rather be due to an increase in the rate of hydrolysis of the internal amide side-chains of keratin.

In contrast to all the other treatments tested, the inclusion of nickel ammonium hydroxide or ethanol resulted in more rapid penetration of zinc and azide ions through hard hoof horn than through soft hoof horn. This effect of ethanol may result from its destabilization of the high glycinetyrosine

containing proteins in hard keratins. Nickel ammonium hydroxide may act by breaking hydrogen bonds within keratin. However, another hydrogen bond breaking reagent, 8M urea, did not increase the penetration of hoof horn by azide. The treatment of footrot in sheep that have dry, hardened feet may be improved by the addition of agents that increase penetration through hard hoof horn. This work is supported by the Australian Wool Research Trust Fund.

EXAMPLE 2

In Vivo Testing

Extensive testing of chemicals for penetration and uptake into the ovine hoof identified a few chemicals (Example 2) that showed potential for footrot treatment. Further experiments to determine the toxicity of these chemicals to *B. nodosus* were conducted. When factors such as practicability for field use, cost, toxicity and adverse effects on wool were considered the most promising treatment was a combination of zinc sulphate and sodium lauryl sulphate. This treatment has been tested on severely footrot affected sheep in pen and paddock trials. Sheep were exposed to the treatment for varying periods. Best results were produced if the treatment was applied for one hour on two occasions 5 days apart. This treatment regime is being assessed in commercial flocks of 500 to 1000 sheep.

Several pen trials using this treatment have been completed and commercial flock trials involving 500 to 1000 sheep per property are in progress.

Results

The results of penetration and uptake experiments have been that a combination of zinc sulphate and sodium lauryl sulphate was found to be the most potentially useful penetrative treatment.

Bacteroides nodosus has been found to be quite sensitive to zinc ions. Levels of zinc as low as 10 ppm in culture medium will inhibit growth of this organism. However, much higher concentrations than this are required within the hoof to kill the organism. Experiments were conducted using feet from recently slaughtered sheep that had been treated with a zinc solution for different times to attain a range of hoof tissue zinc levels. These feet were then used to prepare hoof agar culture plates. A sufficient amount of zinc could in fact accumulate within the hoof to kill *B. nodosus*. At concentrations above 400 ppm (μg Zn^{++}/g wet weight hoof horn) *B. nodosus* did not grow and could not be recovered as a viable organism from these cultures plates. Concentrations of Zn^{++} greater than 400 ppm can be achieved if feet are treated with a zinc sulphate/sodium lauryl sulphate solution for one hour.

The treatment solution was also tested for stability and activity in the presence of organic contamination. Treatment solution containing 20% w/v sheep faeces and left at room temperature for four weeks did not show any significant decline in zinc concentrations or in bacteriocidal activity against *B. nodosus*.

Efficacy and Safety

Efficacy. Pen trials

Footrot was induced in 15 merino weaners by lightly scoring their interdigital skin with a dissecting needle and holding the group in a pen with 2 infected sheep on wet foam rubber mats. Serological testing on isolates of *B. nodosus* from these sheep showed them to belong to serogroup A. Footrot was allowed to progress until at least 3 feet on each animal had severe (3 and 4 score) lesions. The sheep were then randomly divided into 3 groups of 5 and these groups received the following treatment:

(a) Experimental treatment group:
This group was treated by footbathing in the formulation for one hour on two occasions 5 days apart. No footparing was performed.

(b) Formalin treatment group:
This group was treated by footbathing in 10% v/v formalin for 10 minutes on two occasions 5 days apart. No footparing was performed.

(c) Control group:
This group received no treatment. No footparing was performed.

Sheep in groups (a) and (b) were placed in clean pens on wet foam rubber matting after the first footbathing and were returned to the same pens after the second footbathing. Sheep in the control group were placed in a clean pen on wet foam rubber matting at the same time as groups (a) and (b). The warm ambient temperature (11°C—28°C) combined with the wet environment made conditions ideal for the spread and progression of footrot after treatment. Results of this trial are summarized in the table below:

Post Treatment		Number of Feet Affected (Total Footscore)					
Treatment	No. of Sheep	Day 0	Day 7	Day 14	Day 21	Day 28	Days from Treatment to Breakdown*
(a) Formulation	5	17(57)	0	0	0	0	No breakdown up to 42 days
(b) Formalin	5	19(68)	0	13(36)	15(45)	17(58)	>14 days
(c) Control	5	17(64)	18(68)	19(59)	17(59)	18(67)	—

*Breakdown is defined as a visible active underrunning lesion and identification of *B. nodosus* from that lesion.

Each foot of every sheep was thoroughly examined at weekly intervals for a total of 7 weeks. Formalin footbathing lasted for only 10 minutes as prolonged exposure can result in considerable damage to the feet (Littlejohn 1972; Pryor 1959). Foot lesions were evaluated using the scoring system of Egerton and Roberts (1971).

When treating sheep with severe footrot by footbathing without prior footparing, the new formulation was greatly superior to formalin. Sheep treated with the formulation were completely cured of footrot and all lameness had disappeared 7 days after treatment. Formalin treated sheep remained lame and active footrot was evident 14 days after treatment. Sheep treated with the new formulations appeared to suffer no discomfort while standing in the footbath. Sheep standing in the formalin footbath were clearly distressed and repeatedly lifted feet out of the formalin. It is worth noting however that the condition of feet prior to treatment was not completely representative of field situations. Sheep used in pen trials had continually wet feet for 4 weeks prior to treatment. This softens the feet and may have enhanced the penetration of zinc (from the formulations) and formalin into the feet.

Conclusion

A complete cure of severe footrot was achieved by using two one hour footbathing treatments given five days apart using the new formulation. Recovery from lameness occurred in less than 7 days. Formalin failed to cure or alleviate lameness due to footrot.

Field Trials

Treatment trials on 3 commercial sheep flocts at property A, Glenaladale, Bairnsdale Shire, Victoria, involving approximately 3000 sheep have been conducted. The treatment consisted of two, one hour footbathings with the formulation given 5 days apart. After the first footbathing treated sheep were placed in a clean paddock (no other sheep for at least 7 days). Sheep were returned to this or another clean paddock after the second treatment. Control sheep were held in one similar paddock throughout the 12 week duration of the field trials although this paddock had not necessarily been free of sheep for the previous 7 days. In all field trials normal stocking rates and management practices prevailed as far as possible.

6000 ewes, most of them with lambs at foot, were treated on this property. Footrot was diagnosed by standard laboratory procedures. The disease was of recent occurrence (few 3 or 4 score feet) but was rapidly spreading at the time of treatment. Weather conditions during the course of the trial were very dry and a considerable degree of natural remission occurred. Isolates of *B. nodosus* from this property were serotyped as group A.

Sheep were treated on 20 July 1982 and 27 July 1982 with the formulation. No footparing was performed. Prior to treatment 80 ewes were selected at random and their feet thoroughly individually examined. Fifty-nine percent were found to be affected with footrot and 23% of affected sheep had 3 or 4 score lesions. Forty of these ewes were placed in a separate paddock for the remainder of the trial. These sheep acted as controls. The remaining 40 sheep were treated with the rest of the flock but after treatment were placed in a separate paddock for the remainder of the trial. These sheep acted as a subsample of the treated flock and were thoroughly examined at 6 and 12 weekly intervals post treatment. The remainder of the flock was examined 7 weeks post treatment at shearing time. Results of the control and treatment subgroups are shown in the table below.

No footrot could be detected in the remainder of the treated sheep 7 weeks post treatment. As at 10 months post-treatment, no cases of footrot have been identified from this property despite good falls of rain over the last 3 months. Some problems arose while treating ewes with young lambs at foot. Due to the long treatment time in the footbath some lambs attempted to drink from their mothers and became completely immersed in the formulation. These lambs suffered reddening of the

membranes around the eyes, however there were no deaths and on inspection two weeks later there was no corneal opacity or inflammation around the eyes.

In this trial the formulation was able to completely cure sheep that had experienced a recent outbreak of footrot, however, over most of the course of this trial climatic conditions were not favourable to the spread of footrot. While the incidence was high severity of the disease was low. Very few sheep had abnormal and excessive hoof growth that is seen in sheep that have carried the disease for more than one season. A striking observation was that treated sheep recovered from lameness within a week of treatment.

Time	Group	Number of Sheep	Number Affected (%)	Number Affected Feet (%)	Number Affected with 3 or 4 Score (%)	Percent of Feet Recovered
Pre-treatment 20 July 1982	Treated	40	22(55)	37(23)	14(38)	—
	Control	40	25(63)	45(28)	4(9)	—
6 weeks post treatment	Treated	40	0	0	0	100%
	Control	40	25(65)	50(31)	2(4)	0%
12 weeks post treatment	Treated	40	0	0	0	100%
	Control	40	11(28)	18(116)	0	60%

On a property B at Goon Nure, Bairnsdale Shire, Victoria, approximately 2100 mixed age ewes and merino weaners were treated over several days starting on 18 November 1982. Isolates of *B. nodosus* from the property belonged to serogroup A. This property has had a long history of footrot and this combined with the very dry conditions resulted in many of the sheep having very overgrown, misshapen and hard feet. Due to the large number of sheep in this trial it was not practical to footscore and identify every sheep so a subgroup of 50 were randomly selected from the main mob, ear tagged and footscored to assess severity and incidence in the flock. These sheep then acted as untreated controls for the remainder of the trial. Starting 2 weeks after treatment the treated sheep were examined until all had been seen by 12 weeks after treatment.

The treatment regime was identical to the pen trials and property A trial. The results are summarized below.

There was a very marked remission of footrot in the control group over the 12 weeks of the trial no doubt due to the very hot dry conditions. Because of this it is difficult to assess the effectiveness of treatment, however two things can be deduced from the data; the treatment substantially reduced the incidence of footrot but did not cure all sheep. Those sheep that remained uncured all had grossly misshapen and overgrown feet and in all cases the lesion was in the toe region. As was observed in property A treated sheep recovered from lameness within one week while affected sheep remained lame throughout the trial.

Time	Group	Number of Sheep	Number Affected (%)	Number Affected Feet (%)	Number Affected Feet with 3 or 4 Score (%)	Percent Feet Recovered
Pretreatment	Control	50	28(56)	48(24)	14(29)	—
12 weeks post treatment	Control	50	8(16)	8(4)	2(25)	83
	Treated	2000	15(0.75)	15(0.2)	15(100)	99.2*

*Based on pretreatment incidence in control group.

243 mature Romney Marsh ewes and rams at property C at Scotts Creek, Camperdown District, were involved in this trial in Western Victoria. Sheep on this property were infected with *B. nodosus* serogroup F. All sheep were individually identified and foot scored prior to treatment. This property was not affected by drought and there was adequate pasture feed available. Good rains fell over the last 8 weeks of this trial providing suitable conditions for the spread and progression of footrot.

Treatment regime was identical to that described for the previous trials except that 11 sheep were removed at the initial inspection. These sheep had cronic footrot with severely misshapen and overgrown feet. Results of this trial are summarized in the table below.

Despite wet conditions for most of the trial there was still a significant degree of remission in the

control sheep, however the cure rate for treated sheep was much greater. As with property B, treated sheep that remained infected had misshapen overgrown feet and the active lesion was invariably in the toe region. Treated sheep recovered from lameness within one week.

Time	Group	Number of Sheep	Number Affected (%)	Number Affected Feet (%)	Number Affected Feet with 3 or 4 Score (%)	Percent Feet Recovered
Pretreatment	Control	46	26(57)	38(21)	20(53)	—
	Treated	193	109(56)	159(21)	84(53)	—
6 weeks post treatment	Control	42	20(48)	28(17)	18(64)	22
	Treated	190	*6(3)	6(.08)	6(100)	96
12 weeks post treatment	Control	42	15(36)	16(9.5)	14(88)	56
	Treated	181	3(1.7)	3(0.4)	3(100)	94

*These sheep were removed from the treated group at 6 week inspection.

Conclusions

The above field and pen trials indicate that the new formulation is highly effective footbathing treatment for footrot. The treatment produces a greater than 90% cure rate on severely affected sheep without any footparing being done. In sheep with a recent outbreak of footrot, when hoof overgrowth and deformity is not present, an even higher cure rate could be expected. The treatment cannot however be expected to eradicate footrot in all instances as some sheep, particularly those with misshapen and overgrown feet will not be cured by one course of treatment.

In all trials the formulation produced a rapid recovery from lamaness due to footrot. The great majority of affected sheep were fully mobile 3 to 7 days after completion of treatment.

Safety

(a) Intended Recipients, Sheep:

During field and pen trials when approximately 3000 sheep and lambs were treated the only adverse reaction noted was inflammation around the eyes to lambs that became completely immersed in the footbath. This condition had disappeared within two weeks without remedial action being taken.

A trial was undertaken to observe any adverse reactions in sheep treated with *double* strength formulation.

Experimental Animals:

Twenty merino sheep were used for this trial. These animals ranged in age from 14 months to 6 years, body condition ranged from emaciated to good, wool growth was less than 1 cm to 6 cm. Eleven of these sheep had active or chronic footrot.

Treatment:

All sheep were stood in double recommended strength formulation for one hour on two occasions 5 days apart.

Findings:

No adverse reactions were discovered immediately after treatment. One week post treatment 10 sheep were euthanized and postmortem by a veterinary pathologist was performed on each animal. Particular attention was paid to those parts of the anatomy exposed to the formulation. There were no abnormal findings. The interdigital skin was grossly and histologically normal. No corneal opacity could be detected even though some animals had the formulation accidentally splashed into their eyes during treatment. One sheep died 4 days after the first footbathing. A complete post mortem revealed that emaciation was the cause of death and was unrelated to treatment. Tissue zinc levels from this animal were not elevated. Another sheep died 11 days after completion of treatment. Post mortem revealed that cause of death was severe parasite pneumonia and was unrelated to treatment. Tissue zinc levels from this animal were also normal.

The flock from which the sheep used in this trial were purchased was suffering malnutrition due to the drought. Several other sheep from this flock (but not involved in this trial) died on the property at the time of the trial. Sheep from this flock were used despite their emaciated condition because they were the only footrot infected sheep available at the time.

The remaining 8 sheep were euthanized 14 days after completion of treatment and post mortem examinations were performed. Once again there were no abnormal findings and interdigital skin was grossly and histologically normal.

A further trial was conducted to determine whether water deprived sheep would drink the formulation.

Four sheep were used for this experiment. Two sheep were housed in a pen with access to dry feed and a drinking trough containing working strength formulation, the volume of which was recorded (group 1). The other two sheep had access to dry feed only (group 2). Group 2 acted as controls in case of adverse reactions to water deprivation and dry feed. After 64 hours none of the formulation had been drunk by group 1. The sheep in group 1 were then offered water which they began to drink within 5 minutes. As soon as drinking had begun the water was removed and replaced with formulation in an identical container. The sheep approached the trough but would not drink over the next 4 hours. It can therefore be concluded that the formulation is most unpalatable to sheep.

(b) Other Domestic Animals:

A cross-bred dog was stood in a footbath containing the formulation (10 cm deep) so that its feet were immersed for two one minute periods. Close examination of the dogs feet did not reveal any adverse reactions to this exposure.

(c) As outlined in the Toxicology section of this submission zinc is ubiquitous and has a low toxicity to a wide range of animals tested. The formulation is only for use in footbaths which are usually located within sheepyards; therefore access to most animals is greatly restricted. It is very unlikely that animals (including birds) that do gain access would drink the formulation as it has proven unpalatable to sheep. Accidental immersion in the formulation is also unlikely to produce poisoning as sheep and lambs that were immersed suffered only minor transient effects. High levels of zinc are toxic to aquatic life however due to the fact that the formulation can be reused (therefore minimal disposal problem) and that it is not likely to be used immediately adjacent to waterways, this hazard is low.

Finally, it is to be understood that various other modifications and/or alterations may be made without departing from the spirit of the present invention as outlined herein.

CLAIMS

1. A veterinary composition for the treatment of ovine footrot, including an effective amount of:
(a) a zinc salt, and
(b) a fatty thioacid or derivative thereof.

2. A composition according to claim 1, wherein said zinc salt is soluble in said effective amount in water, alcohol or mixtures thereof.

3. A composition according to claim 1 or claim 2, wherein said zinc salt is a zinc acid salt, a derivative thereof, or a mixture of at least two thereof.

4. A composition according to claim 3, wherein said zinc salt is a zinc halide selected from zinc oxy-halides such as zinc perchlorate, zinc chloride, zinc bromide and zinc iodide, a derivative thereof, or a mixture of at least two thereof.

5. A composition according to claim 4, wherein said zinc salt is zinc chloride.

6. A composition according to claim 3, wherein said zinc salt is a zinc thioacid salt.

7. A composition according to claim 6, wherein said zinc salt is selected from zinc sulphite, zinc hyrdosulphite, zinc sulphate, zinc sulphonate, zinc hydrosulphite, zinc hydrosulphate, derivatives thereof, or a mixture of at least two thereof.

8. A composition according to claim 7, wherein said zinc salt is zinc sulphate monohydrate or zinc sulphate heptahydrate.

9. A composition according to claim 3, wherein said zinc salt is selected from zinc acetate, zinc nitrate, zinc ammonium chloride, zinc carbonate, zinc borate, zinc ethyl sulphate, zinc phenol sulphonate, zinc salicylate, zinc hydroxyhydrosulphate, and mixtures thereof.

10. A composition according to any one of claims 1 to 9, further including a solvent, said zinc salt being present in a concentration of from about 2% wt./vol. to about 100% wt./vol.

11. A composition according to any one of claims 1 to 8, wherein said composition is a solid in which said zinc salt is present in a concentration from about 80% wt./wt. to about 98% wt./wt.

12. A composition according to any one of claims 1 to 11, wherein said fatty thioacid or derivative thereof as one functioning to potentiate the absorption of zinc ions into ovine hoof horn.

13. A composition according to claim 10, wherein said fatty thioacid or derivative thereof is present in a concentration of from about 0.4% wt./vol. to about 10% wt./vol.

14. A composition according to claim 11, wherein said fatty thioacid or derivative thereof is present in a concentration of from about 2% wt./wt. to about 20% wt./wt. of active ingredients.

15. A composition according to any one of claims 1 to 9, 11, 12 or 14, wherein said composition is a solid including an effective amount of a solubilizing agent.

16. A composition according to claim 15, wherein said solubilizing agent is a bisulphate salt such as sodium hydrogen sulphate.

17. A composition according to claim 16, wherein said solubilizing agent is present at a concentration of from about 1% wt./wt. to about 2% wt./wt. of active ingredients.

18. A composition according to any one of claims 1 to 17, wherein said fatty thioacid or derivative thereof is a lauric acid derivative, or a mixture of at least two thereof.

19. A composition according to claim 18, wherein said lauric acid derivative is a lauryl sulphate or lauryl ether sulphate salt, or a mixture of at least two thereof.

20. A composition according to claim 19, wherein said lauryl sulphate or lauryl ether sulphate salt is selected from alkali metal, alkaline earth metal, ammonium and amine salts thereof, and mixtures thereof.

21. A composition according to claim 20, wherein said lauryl sulphate salt is selected from sodium lauryl sulphate, potassium lauryl sulphate, magnesium lauryl sulphate, a corresponding lauryl ether sulphate and mixtures thereof.

22. A composition according to claim 20, wherein said lauryl sulphate is selected from ammonium lauryl sulphate, monodi- or tri-ethanolamine lauryl sulphate, triethanolamine ammonium lauryl sulphate, monoisopropylamine lauryl sulphate, a corresponding lauryl ether sulphate and mixtures thereof.

23. A composition according to any one of claims 1 to 22, further including as an enhancing agent an azide compound.

24. A composition according to claim 23, wherein said azide compound is an alkali metal azide such as sodium azide.

25. A composition according to any one of claims 1 to 22, further including as an enhancing agent an alcohol such as ethanol or nickel ammonium hydroxide.

26. A method for the treatment of footrot in ovine animals which includes topically administering a veterinary composition according to any one of claims 1 to 25.

27. A method according to claim 26, wherein the treatment includes subjecting ovine animals to a foot bath containing said composition.

28. A method according to claim 27, wherein the treatment is conducted so as to attain a mean concentration of not less than 500 μgm zinc ions/gm wet weight of hoof horn in said animals.

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